Rejection of Claims 1-9 and 10-15 Under 35 U.S.C. § 112, Second Paragraph

Claims 1-9 and 10-15 were rejected under 35 U.S.C. § 112, second paragraph on the ground that the phrase "an elevation in levels" is indefinite because it is unclear as to what the levels are compared to. Applicants have amended claims 1 and 10 to specify that the levels of Pin1 in the test sample are being compared to Pin1 levels in a control sample. The use of controls are a standard art recognized method for establishing whether alterations in experimental sample are present.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-9 and 10-15.

Rejection of Claims 1-26 Under 35 U.S.C. § 112, First Paragraph

Claims 1-26 were rejected under 35 U.S.C. § 112, first paragraph as "containing subject matter which was not described in the specification in such a way as to enable one of skill in the art to which it pertains to make and/or use the invention."

First, the Office Action states that the instant application

> Contemplates the use of nucleic acid molecules, Pin1 protein and antibodies to Pin1 for detection but does not provide guidance in terms of how to assess the levels and what levels are needed to differentiate between abnormal versus normal levels of cell growth.
>
> And further,
>
> [t]he instant application fails to provide specific methodological steps or procedures for which the instant method can or is intended to be used for detecting abnormal cell growth. It is known to those skilled in the art that detection of abnormal cell growth (either benign or malignant) is often difficult and unpredictable in terms of accuracy, and it was also known at the time the invention was made that the art also fails to establish with great certainty the effectiveness of any specific detection method.

Applicants respectfully traverse this rejection for the following reasons.

Applicants provide detailed teachings as to how one of skill in the art would measure Pin1 in a test sample.

Applicants teach methods of assessing the levels of Pin1 nucleic acid and polypeptides in these test samples. Beginning at page 31, line 14 of the specification

Applicants teach preferred methods of detecting and measuring Pin1 levels in a test sample. Applicants specifically teach common methods of detecting Pin1 mRNA or DNA (e.g., through the use of a nucleic acid probe, northern blots, or PCR.), and Pin1 protein (e.g., through the use of antibody based methods including, western blots, radioimmunoassays, enzyme-linked immunosorbent assays, diffusion based Ouchterlony, or rocket immunofluorescent assays) that were generally known and practiced at the time of the instant invention. Applicants further teach at page 31, line 31 how one of skill in the art would make antibodies to be used in the antibody based detection methods of the present invention. Applicants further teach at page 31, line 14 how a skilled artisan would use nucleic acid probes to detect DNA or mRNA levels in a test sample.

Using the teachings in Applicants specification, a ordinary skilled artisan would be able to measure the amount of Pin1 protein or DNA in a biological sample isolated from a subject.

For Example, Applicants teach, beginning at page 32, line 16, that test samples to be used in the methods of the current invention "include samples obtained from a mammal or a subject containing Pin1 which can be used within the methods described herein, *e.g.*, tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject. Typical samples from a subject include tissue samples, tumor samples, blood, urine, biopsies, lymph, saliva, phlegm, pus, and the like." Once this quantitation is done, the determination of whether there is Pin1 overexpression is only a matter of comparing the amount of Pin1 in the test sample with the amount of Pin1 in a control sample. For an ordinary skilled artisan, this would hardly require undue experimentation.

In addition to the above mentioned teachings in Applicants specification, Applicants provide, in Examples 1-3, a detailed analysis of Pin1 protein overexpression in tumor cells indicating that Pin1 is an accurate marker for prostate, colon and breast cancer. Further, in Example 4 examination of a panel of 30 human tissues indicated that levels of Pin1 correlated with proliferative status of the tissue.

Moreover, while the working examples in the instant application are directed to immunohistochemical analyses, this is insufficient to require Applicants to limit the claims to such assays. Applicants have provided detailed description of the methods for

determining the levels of Pin1 nucleic acids, for example, at page 32, where the Applicants disclose the use of Northern Blots to quantitate the amount of DNA in a sample. In short, there is no sound scientific reasoning provided in the Office Action to support an assertion that detection methods for using Pin1 nucleic acids would not adequately detect and elevation in Pin1 levels.

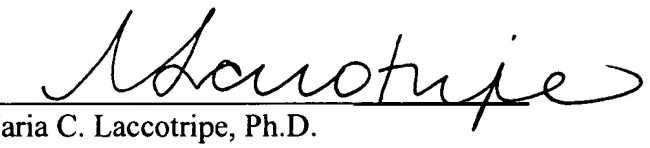
Thus, to require Applicants to limit the claims to the specific embodiments demonstrated by the working examples would unduly limit the scope of protection to which Applicants are entitled. Further, the effectiveness of using Pin1 levels as a means of detecting abnormal cell growth has been shown by Applicants to be both predictable and reproducible.

Based on the above teachings from Applicants specification and the knowledge generally available at the time of the invention, a skilled artisan would be able to practice the methods of the instant invention using only routine experimentation. Accordingly, Applicants respectfully request the reconsideration and withdrawal of the forgoing rejection.

SUMMARY

If a telephone conversation with Applicants' attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' attorney at (617) 227-7400.

Respectfully submitted,



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Appendix A
Version with Markings to Show Changes Made

The specification starting at page 1, line 5 has been amended as follows:

This application claims priority to U.S. provisional Application ~~(~~Serial No.: 60/167,800~~)~~, filed on November 29, 1999 and entitled "Pin1 As A Marker For Abnormal Cell Growth", and to U.S. provisional Application ~~(~~Serial No.: 60/~~XXX,XXX~~ 253,676, filed on November 28, 2000 and entitled "Pin1 As A Marker For Abnormal Cell Growth", the contents of which are incorporated herein in their entirety by this reference. This application is related to PCT application PCT/US00/~~XXXXX~~32560, filed on even date herewith and entitled "Pin1 As A Marker For Abnormal Cell Growth", the entire contents of which is incorporated herein in their entirety by this reference.

Claims 1 and 10 have been amended as follows:

1. A method of detecting abnormal cell growth in a mammal, comprising assessing the level of Pin1 in a test sample from the mammal, wherein an elevation in the levels of Pin1 when compared to a control sample is indicative of abnormal cell growth.

10. A method of detecting abnormal cell growth in a mammal, comprising the steps of:

(a) detecting a level of Pin1 in a test sample; and

(b) comparing the level of Pin1 in the test sample with a control ~~level~~ sample,

and wherein a difference in the level of Pin1 in the test sample when compared to a control sample is indicative of abnormal cell growth in the mammal.

Appendix B

1. (Amended) A method of detecting abnormal cell growth in a mammal, comprising
assessing the level of Pin1 in a test sample from the mammal, wherein an elevation in the levels of Pin1 in said mammal when compared to a control sample is indicative of abnormal cell growth.

2. The method of claim 1, wherein the level of Pin1 is a protein level.

3. The method of claim 1, wherein the level of Pin1 is a nucleic acid level.

4. The method of claim 1, wherein the test sample is an epithelial cell test sample.

5. The method of claim 1, wherein the test sample is a body fluid test sample selected from the group consisting of a blood, ascites, or brain body fluid test sample.

6. The method of claim 1, wherein the abnormal cell growth is benign.

7. The method of claim 1, wherein the abnormal cell growth is a malignant cancer.

8. The method of claim 7, wherein the cancer selected from the group consisting of breast, ovarian, prostatic, cervical, skin, digestive track or testicular cancer.

9. The method of claim 7, wherein the cancer is colon cancer.

10. A method of detecting abnormal cell growth in a mammal, comprising the steps of:

(a) detecting a level of Pin1 in a test sample; and
(b) comparing the level of Pin1 in the test sample with a control sample

and wherein a difference in the level of Pin1 in the test sample when compared to a control sample is indicative of abnormal cell growth in the mammal.

11. The method of claim 10, wherein the level of Pin1 is a protein level.

12. The method of claim 10, wherein the level of Pin1 is a nucleic acid level.

13. The method claim 10, wherein the abnormal cell growth is a malignant cancer.

14. The method claim 13, wherein the cancer is selected from the group consisting of breast, ovarian, prostatic, cervical, skin, digestive track, lung, kidney, liver or testicular cancer.

15. The method of claim 13, wherein the cancer is colon cancer.

16. A method of detecting abnormal cell growth in a mammal by assessing the level of Pin1 protein in a test sample from the mammal, comprising the steps of:

(a) contacting the test sample with an antibody having specificity for Pin1 under conditions suitable for binding of the antibody to Pin1 thereby resulting in the formation of a complex between the antibody and Pin1;

(b) detecting the complex between the antibody and Pin1; and

(c) comparing the amount of the complex in the test sample with an amount of a complex in a control sample,

wherein an elevation in the amount of the complex between the antibody and Pin1 in the test sample compared to the complex in the control sample is indicative of abnormal cell growth.

17. The method of claim 16, wherein the antibody is a polyclonal antibody.

18. The method of claim 16, wherein the antibody is a monoclonal antibody.

19. The method of claim 16, wherein the abnormal cell growth is a malignant cancer.

20. The method of claim 19, wherein the cancer is selected from the group consisting of breast, ovarian, prostatic, cervical, skin, digestive track, lung, kidney, liver or testicular cancer.

21. The method of claim 19, wherein the cancer is colon cancer.

22. The method of claim 16, wherein the antibody is detectably labeled.

23. The method of claim 22, wherein the detectable label is selected from the group consisting of a radioactive, enzymatic, biotinylated and fluorescent label.

24. The method of claim 23, wherein the complex is detected by incubating the complex with a second antibody specific for the complex, wherein the secondary antibody comprises a detectable label.

25. A method of detecting abnormal cell growth in a mammal, comprising the steps of:

a) detecting a level of Pin1 nucleic acid in a test sample; and

b) comparing the level of Pin1 in the test sample with a level of Pin1 in a control sample,

wherein an elevation in the level of Pin1 in the test sample compared to the control sample is indicative of abnormal cell growth.

26. The method of claim 25, wherein the method further comprises performing a polymerase chain reaction with oligonucleotide primers capable of amplifying the Pin1 nucleic acid prior to detection.